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| APPLICATION NO.  | FILING DATE | FIRST NAMED INVENTOR | ATTORNEY DOCKET NO. | CONFIRMATION NO. |
|--|-------------|----------------------|---------------------|------------------|
| 09/784,553   | 02/16/2001  | Ming-Ming Zhou       | 2459-1-003 CIP      | 3124             |
| 23565  | 7590        | 01/26/2005           | EXAMINER            |                  |
| KLAUBER & JACKSON<br>411 HACKENSACK AVENUE<br>HACKENSACK, NJ 07601 |             |                      | LUCAS, ZACHARIAH    |                  |
|  |             |                      | ART UNIT            | PAPER NUMBER     |
|  |             |                      | 1648                |                  |

DATE MAILED: 01/26/2005

Please find below and/or attached an Office communication concerning this application or proceeding.

|                              |                                    |                         |  |
|------------------------------|------------------------------------|-------------------------|--|
| <b>Office Action Summary</b> | <b>Application No.</b>             | <b>Applicant(s)</b>     |  |
|                              | 09/784,553                         | ZHOU ET AL.             |  |
|                              | <b>Examiner</b><br>Zachariah Lucas | <b>Art Unit</b><br>1648 |  |

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

#### Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

#### Status

- 1) Responsive to communication(s) filed on 02 December 2004.
- 2a) This action is FINAL.                    2b) This action is non-final.
- 3) Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

#### Disposition of Claims

- 4) Claim(s) 1-36 is/are pending in the application.
- 4a) Of the above claim(s) 1-4 and 9-36 is/are withdrawn from consideration.
- 5) Claim(s) \_\_\_\_\_ is/are allowed.
- 6) Claim(s) 5-8 is/are rejected.
- 7) Claim(s) \_\_\_\_\_ is/are objected to.
- 8) Claim(s) \_\_\_\_\_ are subject to restriction and/or election requirement.

#### Application Papers

- 9) The specification is objected to by the Examiner.
- 10) The drawing(s) filed on \_\_\_\_\_ is/are: a) accepted or b) objected to by the Examiner.  
Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).  
Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).
- 11) The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

#### Priority under 35 U.S.C. § 119

- 12) Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).
- a) All    b) Some \* c) None of:
1. Certified copies of the priority documents have been received.
  2. Certified copies of the priority documents have been received in Application No. \_\_\_\_\_.
  3. Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

\* See the attached detailed Office action for a list of the certified copies not received.

#### Attachment(s)

- 1) Notice of References Cited (PTO-892)  
2) Notice of Draftsperson's Patent Drawing Review (PTO-948)  
3) Information Disclosure Statement(s) (PTO-1449 or PTO/SB/08)  
Paper No(s)/Mail Date \_\_\_\_\_.

- 4) Interview Summary (PTO-413)  
Paper No(s)/Mail Date. \_\_\_\_\_.  
5) Notice of Informal Patent Application (PTO-152)  
6) Other: \_\_\_\_\_.

**DETAILED ACTION**

1. Currently, claims 1-36 are pending in the application. In the prior action, mailed on August 10, 2004, claims 5-8 were rejected, and claims 1-4 and 9-36 were withdrawn as to non-elected inventions. In the Response, filed on December 2, 2004, the Applicant amended claims 5-8.
2. Claims 5-8 are pending and under consideration to the extent that they read on the elected subject matter or are generic thereto.
3. Because this action raises a new ground of rejection, it is being made Non-Final.
4. The Declaration of Ming-Ming Zhou under 37 CFR 1.132, filed on November 9, 2004 has been considered by the Office. The declaration is insufficient to overcome the rejection of claims 5-8 based upon 35 U.S.C. 112 paragraph 1 as set forth in the last Office action for the reasons set forth in the response to the arguments in traversal of the rejections below.

*Sequence Listing*

5. In the prior action, the application was objected to because the sequences in the specification did not appear to match that of the sequence listing. In view of the submission of the July 19 2004 sequence listing, and the correction made therein, the objection is withdrawn.

*Claim Rejections - 35 USC § 101*

6. 35 U.S.C. 101 reads as follows:

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Whoever invents or discovers any new and useful process, machine, manufacture, or composition of matter, or any new and useful improvement thereof, may obtain a patent therefor, subject to the conditions and requirements of this title.

7. **(Prior Rejection- Withdrawn)** Claims 5-8 were rejected under 35 U.S.C. 101 because the claimed invention is directed to non-statutory subject matter. In view of the amendment of the claims such that they now read on an isolated peptide, thus indicating that the claimed peptides must be isolated from their native environment, the rejection is withdrawn.

8. **(Prior Rejection- Maintained)** Claims 5-8 are rejected under 35 U.S.C. 101 because the claimed invention lacks patentable utility. The claims were also rejected as lacking enablement because, by not providing a sufficient utility for the claimed inventions, the Applicant has not enabled those in the art to use the claimed invention. These claims broadly read on any peptides comprising a sequence according to the generic formula of SEQ ID NO: 3, or on peptides comprising SEQ ID NO: 19.

It is first noted that the Applicant has made no attempt to argue the utility of peptides comprising non-naturally occurring ZA-loop type structures falling within the scope of the formula of SEQ ID NO: 3. The rejection is therefore also maintained on this ground.

With respect to the utility rejection over the peptides of SEQ ID NO: 19, the Applicant traverses this rejection solely on the basis of art teaching the association between bromodomains and HIV infection. However, the art teaches HIV Tat protein association only with the bromodomain of PCAF. There are no teachings either in the art or in the application regarding the association of the ZA loop of SEQ ID NO: 19 with HIV, or with any other disease, disorder, or pathogen infection. It is further noted that the application itself provides evidence that the HIV Tat protein does not interact with every bromodomain. See e.g., page 77, lines 14-19. Further,

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the present claims are limited to peptides comprising a ZA loop corresponding to SEQ ID NO: 3.

The sequence of P/CAF, as described on Figure 1 of the application, does not fall within the scope of the claimed inventions. For example, the residue in the P/CAF ZA loop in Figure 1 does not comprise a

Because the assertion that the claimed peptides may be found useful to treat unspecified disorders, or to identify compounds that may be so useful, is not considered a sufficiently specific utility to meet 35 U.S.C. 101 (see MPEP 2107 I- discussion of specific and substantial utility), the Applicant's arguments are not found persuasive.

It is further noted that the Applicant has not provided any additional arguments regarding the enablement rejection appurtenant to the utility rejection. Because the Applicant has not provided any guidance as to what specific use each of the claimed peptides may be applied for, the rejection is maintained.

This rejection is therefore maintained for the reasons above, and the reasons of record.

***Claim Rejections - 35 USC § 112***

9. The following is a quotation of the first paragraph of 35 U.S.C. 112:

The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

10. (**Prior Rejection- Withdrawn**) Claims 5-8 were rejected under 35 U.S.C. 112, first paragraph, as failing to comply with the written description requirement. The claims previously described a genus of inventions comprising peptides comprising the ZA loop of a

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bromodomains, wherein the bromodomains have between 21-40 amino acids. However, the specification teaches that bromodomains have about 110 amino acids, and not 21-40 amino acids. However, the application also teaches that the ZA loop region of the bromodomain is between 21-40 amino acids in length. In view of the amendment of the claims to clarify that it is this region of the bromodomain that is 21-40 amino acids in length, the rejection is withdrawn.

11. **(Prior Rejection- Maintained)** Claims 5-8 are rejected under 35 U.S.C. 112, first paragraph, as failing to comply with the enablement requirement. The claim(s) contains subject matter which was not described in the specification in such a way as to enable one skilled in the art to which it pertains, or with which it is most nearly connected, to make and/or use the invention. These claims read on peptides comprising the ZA loop of protein bromodomains that fall within an indicated generic structure, that of SEQ ID NO: 3.

The claims were rejected as failing to enable the use of the full scope of the claimed peptides. In particular, it is noted that while the application teaches that the peptides may be used to screen for inhibitors of ZL loop-ligand interactions, the application does not teach the ligands for each of the ZA loop structures that fall within the scope of the claims, nor does the application provide a description of what inhibitors of each of the ZA loop interactions may be used for. While the application provides general suggestions that these inhibitors may be used for the treatment of various diseases, neither the application nor the art associates each of the ZA loops (or the bromodomains from which they are derived) with a specific disease or disorder.

In traversal of the rejection, the Applicant asserts that the peptides may be screened for modulators, and that the bromodomain of P/CAF is known to associate with the Tat protein of

HIV. Additionally, the Applicant has submitted a declaration of Ming-Ming Zhou (a named inventor of the present application) in support of the enablement of the claimed inventions. However, the identification of a potential use for a single embodiment where the claim has many potential embodiments, the uses for which are not known, is insufficient to enable those in the art to make or use the claims to their full scope.

Further, the Declaration asserts only two specific uses for which the application is enabled: the inhibition of Tat/PCAF interaction, and the screening for compounds that inhibit ZA loop/ligand interactions. There is no discussion in the Declaration of what other specific disorders may be treated with the claimed peptides or compounds identified through their use in screening methods other than inhibition of Tat/PCAF interaction, and no identification of ligands to bromodomains the ligands to which are not known. As stated above, there is no demonstration in the application that each of the peptides according to SEQ ID NO: 3, or the peptides of SEQ ID NO: 19 in specific, has any association with HIV. Rather, the application indicates to the contrary on page 77. Thus, both the application and the Declaration provide a specific potential use for only one of the many embodiments that fall within the scope of the claimed peptides. There is no guidance as to what other *specific* disorders the other peptides may be useful in treating, or for what disorder the peptides may be useful in identifying therapeutic compounds against.

In order to enable the claimed invention, the Applicant must teach how to use as well as how to make the claimed inventions. In the present case, there is no identification or guidance towards the specific use to which every peptide according to SEQ ID NO: 3, or the specific peptide of SEQ ID NO: 19, may be applied. The application does provide a general use- the

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identification of compounds that inhibit ZA loop ligand interactions. However, the application does not teach what specific uses these compounds may be applied for (e.g., what specific disease or disorder a compound that inhibits the interaction of SEQ ID NO: 19 with its ligand would be useful to treat). Thus, to practice the claimed invention to its full extent, those in the art would be required to identify, with only little guidance from the application, 1) the ligands for each of the ZA loops falling within the scope of the claims, 2) what, if any, disease or disorder the bromodomain may be associated with, 3) compounds that inhibit the bromodomain/ligand interaction, and 4) determine which, if any, of those compounds may be useful in the treatment of the unidentified disorders. In view of the limited guidance provided by the application with respect to these determinations, and teachings in the art illustrating the breadth of the claims, and limited knowledge regarding the functions and associations of bromodomains, the application has not provided sufficient information to enable the use of all peptides of SEQ ID NO: 3, or of SEQ ID NO: 19 in particular. The rejection is therefore maintained for the reasons of record, and the reasons above.

***Claim Rejections - 35 USC § 102***

12. The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

A person shall be entitled to a patent unless –

- (a) the invention was known or used by others in this country, or patented or described in a printed publication in this or a foreign country, before the invention thereof by the applicant for a patent.
- (b) the invention was patented or described in a printed publication in this or a foreign country or in public use or on sale in this country, more than one year prior to the date of application for patent in the United States.

13. **(Prior Rejection- Maintained)** Claims 5 and 6 were rejected under 35 U.S.C. 102(a) as being anticipated by Dhalluin et al. (Nature 399:491-96- of record in the July 2002 IDS).

It is first noted that, contrary to the Applicant's statement, the rejection was made under 35 U.S.C. 102(a), and not under 35 U.S.C. 102(b).

The Applicant traverses the rejection on the grounds that rejection is improper because the reference on which the rejection is based was published less than one year from the date of the earliest priority date of the present application, and is a publication by the present inventors. This argument is not found persuasive. A reference is considered to be by another where the reference names as an inventor or author at least one individual other than those named as inventors in the present application. See MPEP 2132.01. This is met in view of the identification of several authors in the reference that are not named inventors in the present application, and vice versa. In order to overcome such a rejection on the grounds that the reference is not "by another" the Applicant may file a declaration under 37 CFR 1.131. Id. Such has not been done in the present application. The Applicant's traversal is therefore not found persuasive. The rejection is maintained for the reasons above, and the reasons of record.

14. **(New Rejection)** Claims 5 and 6 are rejected under 35 U.S.C. 102(b) as being anticipated by Yang et al., Nature 382: 319-24. The claims have been described above. Yang teaches the purification of P/CAF, including a fusion protein of P/CAF with a FLAG epitope. Page 320 left column, and page 321, Figure 2 (Methods portion teaching that "P/CAF, hGCN5 and E1A were expressed as FLAG fusions..."). The reference therefore anticipates the indicated claims.

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15. Claims 5-8 are rejected under 35 U.S.C. 102(b) as anticipated by Denis and Green (Genes Dev 10(3): 261-71). The specification does not set any limits on what a peptide includes, but indicates that the term does include chimeric or fusion polypeptides and proteins. Page 25. Thus, proteins fall within the scope of the indicated claims. Davis and Green disclose a protein, identified as Ring3, comprising the sequence of SEQ ID NO: 19. Page 264, Figure 4B. The reference also teaches the recombinant production of the protein as a fusion with a polyhistidine. Page 265, right column. The reference therefore anticipates the indicated claims.

### *Conclusion*

16. No claims are allowed.

17. The following prior art reference is made of record and considered pertinent to applicant's disclosure. However, while relevant they are also not used as a basis for rejection for the stated reasons.

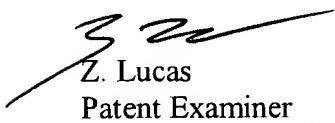
Platt et al., J Virol 73: 9789-95. This reference is relevant in that it teaches fusion proteins comprising portions of the RING3 protein, the protein from which SEQ ID NO: 19 is derived. However, the reference does not teach an isolated peptide comprising SEQ ID NO: 19. The reference also teaches a protein that interacts with RING3. Page 9790. However, this interaction does not occur at the ZA loop. Pages 9791-92.

Taniguchi et al. (Genomics 51: 114-123) and Thorpe et al. (Immunogenetics 44: 391-96). Proteins, disclosed as Ring3 or hsRing3, comprising the sequence of SEQ ID NO: 19 are disclosed in each of the Taniguchi and Thorpe references. However, because it is not clear if the proteins have been isolated, and as the teachings of these references are redundant, in part, to the teachings of Davis and Green above, the references are not applied as prior art.

18. Any inquiry concerning this communication or earlier communications from the examiner should be directed to Zachariah Lucas whose telephone number is 571-272-0905. The examiner can normally be reached on Monday-Friday, 8 am to 4:30 pm.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, James Housel can be reached on 571-272-0902. The fax phone number for the organization where this application or proceeding is assigned is 703-872-9306.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see <http://pair-direct.uspto.gov>. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free).



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